REMARKS/ARGUMENTS

Claims 3-5 are pending in the application. Claims 1, 2, and 6-9 were withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected invention. With this Amendment, Applicants amend claim 3 to be in independent form and adds new claims 10-23. Like claims 3-5, the new claims are drawn to the same elected group: a method for producing Fv-LDP-AE. Claims 3-5 have been further amended to correct informalities regarding abbreviations and to improve their clarity.

In the September 26, 2008 Office action, the Examiner rejected claim 3 as being indefinite as to what is meant by LDM. Applicants have amended claim 3 to include the term lidamycin, clarifying the reference to LDM. The Examiner also rejected claim 5 as being indefinite for the term "preferably." Applicants have amended claim 5 by removing the term "preferably."

The Examiner has further rejected claims 3-5 as purportedly being obvious over Li et al. (Acta Pharmaceutica Sinica, Vol. 35, No. 7, pp.488-491, 2000) ("Li") in view of Terpe et al. (Appl. Microbiol. Biotechnol., Vol. 60, pp.523-533, epub Nov. 2002) ("Terpe"). Applicants respectfully traverse the rejection and request reconsideration.

Applicants respectfully direct the Examiner's attention to the fusion protein of Li and claim 3 of the instant application. The fusion protein as recited in claim 3 is Fv-LDP with the scFv (FV) at the N-terminus followed by the linker, and then the lidamycin (LDP) with the His_6-tag at the C-terminus. This fusion protein is different from that disclosed in Li, which is LDP-Fv, with the lidamycin (LDP) in the N-terminus followed by the linker, and then the scFv (Fv) in the C-terminus. The position of the components has a profound effect on the folding and action of the individual components, whether it be protein binding, antibody recognition, or enzymatic action. In fact, the IC_{50} for Fv-LDP-AE is $1.65x10^{-16}$ M, while the IC_{50} for LDM-FV disclosed

in Li is $9.5x10^{-15}$, showing a 58-fold stronger cytotoxicity for Fv-LDP-AE against cancer cells compared with LDM-FV. (See page 15 in Specification and page 490 of Li). The difference in cytotoxicity can be partly attributed to the difference in orientation of the fusion protein as well as the high AE content in LDM used for the preparation of the energized fusion protein of the present invention.

Further, the method of the amended claim 3 yields about 30% fusion protein of total protein. This information is also disclosed in the Specification of the instant application at page 10, example 3. The method recited in claim 3 is distinguishable from the method disclosed in Li, as the latter only provides a yield of 8% of total protein. (See page 489 in Li). Further, Li discloses the use of PKFL plasmid and E. Coli JM109, whereas claim 3 recites pET-30a(+) and BL21star. (See page 488 in Li).

In brief, the fusion protein formed by the method recited in claim 3 is quite different from the protein disclosed in Li, with a different orientation and a significant difference in IC_{50}, and the relative yield of the fusion protein is significantly different (about 30% versus 8%). Therefore, the method of claim 3 is patently distinct from the method disclosed in Li. Claims 4 and 5 depend from claim 3 and are also allowable. Accordingly, Applicants request reconsideration and a Notice of Allowance for claims 3-5.

The Examiner has provisionally rejected claims 3-5 on the ground of nonstatutory obviousness-type double patenting in view of claim 4 of copending Application No. 11/587199. Claim 4 of Application 11/587199 discloses a fusion protein VH-LDP that has a heavy chain variable domain, while claim 3 of the instant application recites a method of making a fusion protein Fv-LDP that has a single chain Fv fragment. The Examiner asserts that, because "the instant claims are broadly drawn to a single-chain Fv fragment of a monoclonal antibody against type IV collagenase and therefore the antibody of claim 4 of application 11/587199 falls within the same scope."

However, the scFv fragment is distinguishable from the VH fragment. As described in the Specification of the present application, at page 1, the "[s]ingle-chain antibody (scFv) is the minimal, functional antibody fragment having intact antigen binding site of an antibody by fusing VH to VL via a flexible peptide." The scFv has a binding complement of both VH and VL domains, while the VH has only a single binding domain and does not possess the intact antigen binding site of an antibody. Thus, scFv and VH would have qualitatively different antigen binding properties. In addition, the VH is significantly shorter than the scFv fragment because it does not have the VL fragment and the flexible peptide.

Accordingly, Applicants request that the rejection based on double patenting be withdrawn. A notice of allowance is requested.

Respectfully submitted,
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